INFORMED CONSENT FOR THE PRE-IMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) – PRIMARY AND SECONDARY OUTCOMES

Female patient full name:	
Female patient Date of Birth:	
Clinic ID (female patient):	

Partner full name (if applicable):	
Partner Date of Birth (if applicable):	
Clinic ID (partner):	

This consent is intended for patients who are planning to undergo *in vitro* fertilization (IVF) treatment and want Preimplantation Genetic Testing (PGT) to be performed on cells (biopsies) taken from their embryos. Juno Genetics UK Ltd. (Juno Genetics) is the clinical diagnostic laboratory that will receive the biopsies from the embryos and will perform PGT. A separate consent form regarding the embryo biopsy procedure should be provided by the IVF clinic/laboratory performing the biopsy. Juno Genetics recommends that genetic counselling be offered to the patient(s) prior to signing this form.

What is PGT-A?

PGT-A is a method that aims to identify whether an embryo has the correct number of chromosomes. Chromosomes are minute, rod-like structures, that exist inside cells. The chromosomes are made of DNA and carry the instructions (genes) needed for an embryo to develop normally. Human beings typically have 46 chromosomes, including two X chromosomes in the case of females (46,XX) or one X and one Y chromosome for males (46,XY). Embryos with an incorrect number of chromosomes have increased risks of failing to implant in the uterus, miscarrying or producing a child with a genetic abnormality (for example, Down syndrome). PGT-A can potentially reduce these risks by helping to distinguish embryos with the right number of chromosomes from those that have either too many chromosomes or too few. Embryos that are predicted to have a low risk of a chromosome abnormality can be prioritised for transfer to the uterus. PGT-A typically involves the use of standard methods of *in vitro* fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) to produce embryos. The embryos are usually grown for five to seven days, at which point a few cells are removed (biopsied). The embryos are cryopreserved (frozen) while the cell samples are sent to Juno Genetics. The actual embryos do not leave the IVF clinic. Upon receiving the cells sampled from each embryo, Juno Genetics carries out the analysis of the chromosomes. Alternatives to PGT-A that can be used to look for chromosome abnormalities once a pregnancy has begun, include amniocentesis or chorionic villus sampling.

It is crucial that unprotected sexual intercourse is avoided from 15 days prior to egg collection until after the pregnancy test, carried out approximately two weeks after transfer of embryos to the uterus. Sexual intercourse within this time could lead to an untested embryo producing a pregnancy, invalidating any PGT-A results.

Risks and limitations of PGT-A

- There is a chance that no chromosomally normal embryos will be produced in a cycle of IVF and PGT-A. In such cases, the IVF clinic might recommend that no embryos are transferred.
- PGT-A cannot detect all forms of chromosome abnormality. For example, loss or duplication of pieces of chromosomes, rather than whole chromosomes, are not always detected. For this reason, prenatal testing is recommended to confirm that any pregnancy established after PGT-A is chromosomally normal.
- Since PGT-A only looks for abnormal numbers of chromosomes, it cannot exclude the possibility that an embryo could have other types of genetic abnormalities and/or birth defects, which PGT-A does not detect. In the general population, there is a 3-5% risk that a child will be born with a birth defect or intellectual disability due to genetic and/or non-genetic causes. The use of PGT-A does not reduce that risk.
- For abnormalities involving the loss or duplication of whole chromosomes, PGT-A is more than 98% accurate. However, there remains a small chance that an embryo classified 'negative' following PGT-A could still have an incorrect number of chromosomes. Again, prenatal testing is advisable to confirm the status of any pregnancy.
- While very unlikely, there is a chance that a biopsy sample could be lost or damaged due to a problem within the laboratory or during transportation. In such cases, the number of chromosomes in the cells of the embryo remains unknown. Juno Genetics only assumes responsibility for embryo samples once they arrive at its laboratory.

- There is a chance that Juno Genetics will be unable to obtain a result from a biopsy sample. This can happen if the cells removed from the embryo contain degraded DNA, as well as for various other reasons. This typically affects less than 5% of samples.
- Testing is performed on a sample of cells from the embryo, and while it is expected that these cells are chromosomally the same as the remainder of the cells in the embryo, there is a possibility they are different.
- PGT-A offers no guarantee that pregnancy will occur or that a healthy child (free from all genetic or non-genetic defects) will result.
- With any procedure involving handling of microscopic material, human error can occur, although steps are taken in the laboratory to minimise such risks.
- Like many techniques, PGT-A depends upon equipment. Equipment failure and other problems such as loss of power and natural disasters can potentially occur, resulting in failure to obtain PGT-A results and loss of samples.
- PGT-A involves the testing of a small number of cells from each embryo (embryo biopsy). There is a small chance of contamination with cells or genetic material from other sources. This is a risk of the procedure and, if this occurs, it may result in an incorrect analysis or a failure to obtain a result.

Possible embryo classifications in PGT-A cases include:

- Negative: No abnormalities involving loss or duplication of whole chromosomes or parts of chromosomes were detected in the biopsy sample. The embryo is predicted to have a normal number of chromosomes.
- Positive: Embryos in which the biopsy sample is predicted to have an abnormal number of chromosomes. This may involve loss or duplication of whole chromosomes or pieces of chromosome. These embryos are considered to be at high risk of chromosomal abnormality.
- Mosaic: Embryos where some cells in the biopsy specimen have a 'normal' (46,XY/ 46,XX) number of chromosomes while other cells have an 'abnormal' number of chromosomes.
- No result: No prediction could be made concerning the chromosomes in the embryo. This can be caused by a failure to amplify DNA in the biopsy specimen, contamination of the specimen with DNA from another source, and various other technical problems. In such cases, a second biopsy is recommended, provided the embryo is sufficiently developed.

Incidental findings

Occasionally, PGT-A results may indicate the presence of a chromosome abnormality in one of the two parents, such as a chromosome rearrangement (translocation or inversion) or extra/missing chromosome material (microduplications/microdeletions). If results are suggestive of a parental chromosome abnormality, additional testing may be recommended. The PGT-A method alone, cannot be used to detect all possible parental chromosome abnormalities. If identified during testing, copy number gains and losses above 3Mb will be reported, however this is at the discretion of the Clinical Laboratory Director since some gains/losses are of no clinical significance or are likely to be benign.

Mosaicism: Secondary finding of uncertain significance

This testing may detect secondary finding of uncertain significance, which include results suggestive of the presence of a mixture of normal and abnormal cells (mosaicism). At this time, the clinical significance of these findings is not well understood. According to current scientific evidence, embryos with apparent mosaicism in the biopsy sample have a capacity to implant and produce a child as embryos without mosaicism.
For the PGT-A reports including primary+secondary outcomes, mosaic results will be included in the final PGT-A report.

Publications and research

The information regarding your participation in PGT-A will be kept confidential except if it is required by law or by regulatory bodies. However, in some scenarios the data obtained from your embryos may be published to help advance knowledge in the fields of assisted reproduction and genetics. Such information will not identify you. Results from multiple individual patients/embryos is usually grouped together.

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Your samples

All samples will be kept for 5 years before being discarded. In this time, any leftover material from the cells taken from each embryo may be used for training and quality assurance purposes. If you wish to have your samples discarded sooner, please contact the laboratory.

We request that you allow Juno Genetics to use surplus DNA from embryo biopsy specimens to assist in the development of new and/or improved genetic tests. Such DNA is leftover after PGT-A has been completed. The use of this surplus material has no effect on the treatment you receive and is carried out in an anonymised manner (all personal identification is removed from the sample). Please confirm whether you agree to your leftover samples being used to help Juno Genetics to train staff and create new tests.

☐ **Yes**
☐ **No**

I/we give permission for any surplus DNA, remaining after completion of PGT-A testing, to be used for research and the development of new tests. I understand that before any research takes place, all identifying information will be removed from the sample(s).

By signing this form, you are agreeing to the following statements:

- I/we confirm that I/we have read and understood all the information provided in this form and have had the opportunity to ask any questions regarding this information.
- I/we understand that there is potential for PGT-A to be unsuccessful in giving a result and that there is a small possibility for an embryo classified 'negative' using PGT-A to be affected by a chromosome abnormality.
- I/we understand that PGT-A does not completely remove the risk of having a pregnancy affected by a genetic disorder. I/we understand that prenatal testing (amniocentesis or chorionic villus sampling) is recommended in the event of a pregnancy and I/we can discuss this with a genetic counsellor.
- I/we understand that I/we are voluntarily using this test and may withdraw from the testing at any time by notifying the laboratory in writing of my/our intention to withdraw, and that I/we may withdraw my/our consent to any procedure at any time.

_____ _____
Patient's Signature **Date**

_____ _____
Partner's Signature (if applicable) **Date**

The above patient(s) have been counselled by me and others with respect to the risks and benefits of the various options. The patient(s) appeared capable of understanding the information presented as demonstrated by the discussion and their participation.

_____
Clinician/ Genetic Counsellor Name (if applicable)

_____ _____
Clinician/ Genetic Counsellor Signature **Date**